

Supporting Online Material for

A Genome-Wide Association Study Identifies *IL23R* as an Inflammatory Bowel Disease Gene

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Materials and Methods

Subject ascertainment and diagnostic classification: In all cases, informed consent was obtained using protocols approved by the local institutional review board. Cases and geographically matched controls were ascertained through Baltimore, Chicago, Montreal, Pittsburgh, Los Angeles, and Toronto Genetics Research Centers, with additional age and ethnicity-matched controls provided by the New York Health project. The diagnosis of IBD requires a) one or more symptoms of diarrhea, rectal bleeding, abdominal pain, fever, or complicated perianal disease, b) occurrence of symptoms on two or more occasions separated by at least 8 weeks or ongoing symptoms of at least 6 weeks duration, and c) objective evidence of inflammation from radiologic, endoscopic, and histologic evaluation. Ileal CD involvement was defined as mucosal ulceration, cobblestoning, stricturing or bowel wall thickening from endoscopy reports, barium X-rays, operative reports and/or pathology resection specimen reports.

Genotyping methods: For the genome-wide association studies, approximately 750ng of genomic DNA was used to genotype each sample on the Illumina HumanHap300 BeadChip (Illumina, San Diego) at the Feinstein Institute for Medical Research. Samples were processed according to the Illumina Infinium 2 assay manual. Briefly, each sample was whole-genome amplified, fragmented, precipitated and resuspended in appropriate hybridization buffer. Denatured samples were hybridized on prepared HumanHap300 BeadChips for a minimum of 16 hours at 48°C. Following hybridization, the beadchips were processed for the single base extension reaction, stained and imaged on an Illumina Bead Array Reader. Normalized bead intensity data obtained for each sample were

loaded into the Illumina Beadstudio 2.0 software which converted fluorescent intensities into SNP genotypes. The *IL23R* region genotyping in replication cohorts was performed using primer extension chemistry and mass spectrometric analysis (iPlex assay, Sequenom, San Diego) using Sequenom Genetics Services (Sequenom, San Diego).

Data processing: The data from the genome-wide association studies were used to detect possible relatedness in the case-control cohorts. The Hardy-Weinberg disequilibrium test was performed on the genotype data from controls, and we investigated the relationship between Hardy-Weinberg disequilibrium and genotype yield (call rate). The call rate distribution suggested a 94% genotype completion threshold for inclusion of samples in the genetic association analyses. 94.5% of the samples had call rates \geq 98%, and an additional 1.9 % of samples had call rates between 94-98%. No samples had call rates between 92% and 94%. There were only two affected and three control samples with call rates in the 90-92% range. Below 90% call rates, we observed an increase in heterozygote calls. Lowering the threshold to 90% had little effect on the results of the association studies.

The genotype data from the family-based cohorts were used to determine Mendelian inconsistencies and departures from Hardy-Weinberg equilibrium. We eliminated from the analysis all the families with more than two Mendelian inconsistencies and families that were not informative because a parent or the sole affected offspring failed genotyping. After cleaning, there were 883 nuclear families (875 independent) with both parents and at least one affected offspring genotyped. Eight nuclear families that we analyzed were from the same extended family as another nuclear

family. After zeroing genotypes that produced residual Mendelian inconsistencies, genotype completion rates for each marker in the clean family-based association data ranged from 97.2% to 99.8%.

Statistical analysis: The single marker analyses for the genome-wide data in each ethnic group were done using chi-square tests on allele counts; for all the markers associated at the $P \leq 0.01$ level, Fisher's exact tests on allelic counts were also performed and yielded the P-values reported in the manuscript. To test whether the association signals found in the *IL23R* gene region could arise from untyped variation within the *IL12RB2* gene, we examined linkage disequilibrium patterns of International HapMap SNPs located within the *IL12RB2* gene and IBD-associated *IL23R* region SNPs using International HapMap CEU data (*S1*).

The data from the Jewish and non-Jewish case-control cohorts were analyzed jointly using a Cochran-Mantel-Haenszel chi-squared test (*S2*); we used the test as implemented in R (<http://www.r-project.org/>) with the option that gives an exact P-value. The analyses conditional on Arg381Gln were performed using the Cochran-Mantel-Haenszel test with strata defined based on Arg381Gln genotypes. Note that we combined the Gln/Gln and Arg/Gln genotypes to obtain a single stratum because the glutamine variant is very rare.

For the family-based association analyses, the affection status for each individual study subject in the 883 nuclear families was coded four times to reflect the following four possible phenotype and non-Jewish vs. Jewish ethnicity combinations: non-Jewish and CD-affected, non-Jewish and UC-affected, Jewish and CD-affected, Jewish and UC-

affected. In addition, the affection status was coded for the all IBD (CD, UC, or indeterminate colitis) phenotype. Counts of untransmitted and transmitted alleles from heterozygous parents to affected offspring were determined using the standard transmission/disequilibrium test implemented in the Haplovew software package (<http://www.broad.mit.edu/mpg/haplovew/>) (S3). Chi square- and P-values were computed using an empirical variance-covariance estimator that adjusts for the correlation among sibling marker genotypes, implemented in the FBAT software (<http://www.biostat.harvard.edu/~fbat/fbat.htm>) (S4, S5). The P-values from the case-control and family-based analyses were combined using Fisher's method (S6) to quantify the overall evidence for association.

	372				376				381																				
Human, nucleotide Human, coding	TCT	TTG	ATT	GGG	ATA	TTT	AAC	AGA	TCA	TTC	CGA	CAA	ACT	GG	g	t	a	g	g	t	t	t	t	g	c	a	g	a	
Chimp	Ser	Leu	Ile	Gly	Ile	Phe	Asn	Arg	Ser	Phe	Arg	Gln	Thr	Gly	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Rhesus	Ser	Leu	Ile	Gly	Ile	Phe	Asn	Arg	Ser	Leu	Arg	Gly	Thr	Gly	g	t	a	g	g	t	t	t	t	t	g	c	a	g	a
Mouse	Ser	Leu	Ile	Gly	Ile	Phe	Asn	Arg	Ser	Leu	Arg	Gly	Thr	Gly	g	t	a	g	g	t	t	t	t	t	g	c	a	g	a
Rat	Ser	Leu	Ile	Gly	Ile	Phe	Asn	Arg	Ser	Leu	Arg	Gly	Ile	Gly	g	t	a	g	g	t	t	t	c	t	a	t	ag	-	
Rabbit	Ser	Leu	Ile	Gly	Ile	Phe	Asn	Arg	Thr	Leu	Arg	Gly	Ile	Gly	g	t	a	g	g	t	t	t	c	t	a	t	ag	-	
Dog	Ser	Leu	Ile	Gly	Ile	Phe	Asn	Arg	Ser	Ile	Arg	Gly	Thr	Gly	g	t	a	g	g	t	t	t	t	t	g	t	a	g	a
Cow	Ser	Leu	Ile	Gly	Ile	Phe	Asn	Arg	Ser	Leu	Arg	Gly	Thr	Gly	g	t	a	g	g	t	t	t	c	t	g	t	a	g	a
Armadillo	Ser	Leu	Ile	Gly	Ile	Phe	Asn	Arg	Ala	Leu	Arg	Gly	Thr	Gly	g	t	a	g	g	t	t	t	t	t	g	t	a	a	a
Elephant	Ser	Leu	Ile	Gly	Ile	Phe	Asn	Arg	Ser	Val	Arg	Gly	Thr	Gly	g	t	a	g	g	t	t	t	t	t	g	t	a	g	a
Tenrec	Ala	Leu	Ile	Gly	Val	Phe	Asn	Lys	Ser	Leu	Arg	Gly	Thr	Gly	g	t	a	g	g	-	t	t	t	t	g	a	a	g	a
Opossum	Phe	Leu	Thr	Val	Ile	Phe	Lys	Gln	Ser	Leu	Arg	Gly	Val	AG	G	t	a	a	g	t	g	t	g	t	t	c	a	-	-

Fig. S1. Sequence conservation between species. Exonic nucleotide sequences are in capital letters. Codons 372, 376 and 381 are completely conserved between reference sequences from designated species. Sequence comparisons were obtained using the UCSC Genome comparative genomics browser (<http://genome.ucsc.edu/>) (S7, S8)

Table S1a. Summary of markers for the non-Jewish case-control cohort corresponding to the genomic window shown in Fig. 1. Shown are information about the markers (rs number and base pair position on chromosome 1, Build 35), genotype counts for Crohn's disease (CD) cases and controls, P-values for the Hardy-Weinberg test (HW-P) and Fisher's exact test for allelic counts (Allele-P). Minor allele frequencies (MAF) for cases and controls, odds ratios (ORs) and 95% confidence intervals (CI) for the first allele are shown.

marker	position	Non-Jewish case-control cohort														
		CD genotypes			Control genotypes			HW-P	Allele-P	CD MAF	Control MAF	OR	CI-Lower	CI-Upper		
		1	2	11	12	22	11	12	22							
rs10789220	67263230	A	G	270	229	43	258	235	48	0.59	4.52E-01	0.29	0.31	1.08	0.89	1.30
rs1830513	67287570	A	G	10	138	394	12	129	403	0.66	7.59E-01	0.15	0.14	1.04	0.81	1.34
rs2863202	67296356	A	G	14	163	366	17	155	372	0.86	9.10E-01	0.18	0.17	1.02	0.81	1.27
rs3762318	67309140	A	G	356	163	12	389	132	19	0.068	2.47E-01	0.18	0.16	0.87	0.69	1.10
rs10489631	67313136	A	G	174	283	86	163	257	124	0.24	3.44E-02	0.42	0.46	1.20	1.01	1.43
rs4655683	67323634	A	G	35	227	281	72	232	240	0.18	2.95E-04	0.27	0.35	0.71	0.59	0.86
rs12041056	67339281	A	G	102	286	155	88	269	185	0.55	5.66E-02	0.45	0.41	1.18	0.99	1.40
rs1884444	67345833	A	C	167	284	92	156	263	125	0.49	5.81E-02	0.43	0.47	1.18	0.99	1.40
rs6687620	67360481	A	G	9	143	390	11	109	424	0.21	5.91E-02	0.15	0.12	1.27	0.99	1.65
rs2064689	67365031	A	G	28	204	311	58	221	265	0.24	2.58E-04	0.24	0.31	0.70	0.58	0.85
rs10489630	67374643	A	C	226	263	52	188	260	96	0.71	2.80E-04	0.34	0.42	1.38	1.16	1.65
rs1004819	67382234	A	G	66	274	203	36	233	275	0.15	3.79E-06	0.37	0.28	1.53	1.27	1.84
rs790631	67388943	A	G	262	247	32	288	217	38	0.74	3.63E-01	0.29	0.27	0.92	0.76	1.11
rs7517847	67393690	A	C	241	238	59	164	274	102	0.51	1.09E-07	0.33	0.44	1.61	1.34	1.92
rs2863212	67397137	A	G	435	101	7	432	102	10	0.17	6.80E-01	0.11	0.11	1.07	0.81	1.41
rs7530511	67397408	A	G	9	114	420	10	115	419	0.52	8.96E-01	0.12	0.12	0.98	0.75	1.27
rs10489629	67400370	A	G	207	262	74	145	281	118	0.41	4.27E-06	0.38	0.48	1.49	1.25	1.78
rs2201841	67406223	A	G	194	280	69	274	223	47	0.86	4.57E-06	0.38	0.29	0.66	0.55	0.79
rs11804284	67411275	A	G	9	114	420	10	115	419	0.52	8.96E-01	0.12	0.12	0.98	0.75	1.27
rs12030948	67413786	A	C	78	282	178	76	231	232	0.13	1.47E-02	0.41	0.36	1.25	1.04	1.49
rs11465804	67414547	A	C	519	22	0	475	64	2	0.92	7.52E-07	0.02	0.063	3.23	1.95	5.53
rs10489628	67416128	A	G	65	255	223	93	263	188	0.95	5.47E-03	0.35	0.41	0.78	0.65	0.93
rs11209026	67417979	A	G	0	21	521	3	70	468	0.83	5.05E-09	0.019	0.070	0.26	0.15	0.43
rs6682033	67420691	A	G	310	191	42	260	243	41	0.12	1.87E-02	0.25	0.30	1.26	1.04	1.52
rs1343151	67431150	A	G	47	205	291	63	277	204	0.032	2.26E-06	0.28	0.37	0.65	0.54	0.78
rs10889675	67434237	A	C	3	99	434	10	103	430	0.19	2.63E-01	0.10	0.11	0.85	0.64	1.13
rs10889677	67437141	A	C	69	280	194	44	225	275	0.83	1.82E-06	0.38	0.29	1.55	1.29	1.86
rs7539328	67444624	A	G	39	184	316	69	203	266	0.0029	1.48E-04	0.24	0.32	0.69	0.57	0.84
rs11209032	67452113	A	G	73	280	189	36	247	261	0.026	1.03E-06	0.39	0.29	1.56	1.30	1.87
rs1495965	67465529	A	G	128	285	130	179	282	83	0.10	2.93E-05	0.50	0.41	0.69	0.58	0.83
rs924080	67472161	A	G	180	259	97	125	283	131	0.24	1.19E-04	0.42	0.49	1.40	1.17	1.66
rs12131065	67481027	A	G	25	200	318	30	218	296	0.21	1.77E-01	0.23	0.26	0.87	0.71	1.07
rs3790558	67489042	A	C	168	275	100	148	275	121	0.75	7.77E-02	0.44	0.48	1.16	0.98	1.38
rs10489627	67491697	A	G	252	230	61	232	233	79	0.10	8.59E-02	0.32	0.36	1.17	0.98	1.40
rs2066445	67493996	A	G	19	142	382	18	178	348	0.41	6.61E-02	0.17	0.20	0.81	0.65	1.02
rs1495964	67506839	A	G	201	250	92	179	272	93	0.55	3.16E-01	0.40	0.42	1.09	0.92	1.30
rs3790565	67523377	A	G	361	164	18	360	169	15	0.36	9.56E-01	0.18	0.18	0.99	0.79	1.24
rs3790567	67534398	A	G	35	195	312	28	195	315	0.76	5.45E-01	0.24	0.23	1.06	0.87	1.30
rs3828069	67551594	A	G	379	154	10	359	161	24	0.28	5.56E-02	0.16	0.19	1.25	0.99	1.57
rs4297265	67564356	A	G	198	250	95	174	271	98	0.67	2.58E-01	0.41	0.43	1.11	0.93	1.32
rs2270614	67568042	A	G	96	249	198	98	271	175	0.70	2.77E-01	0.41	0.43	0.91	0.76	1.08
rs7555183	67572648	A	G	48	226	269	62	239	243	0.78	6.49E-02	0.30	0.33	0.84	0.70	1.01

Table S1b. Summary of markers, data and results for the Jewish case-control cohort corresponding to the genomic window shown in Fig. 1. The final column lists the combined P-values (non-Jewish and Jewish cohorts) obtained using the Cochran-Mantel-Haenszel test graphed in Fig. 1.

marker	position	Jewish case-control cohort												Combined			
		CD genotypes				Control genotypes				HW-P	Allele-P	CD MAF	Control MAF	OR	CI-Lower	CI-Upper	
		1	2	11	12	22	11	12	22								
rs10789220	67263230	A	G	199	163	37	230	169	33	0.80	2.76E-01	0.30	0.27	0.88	0.71	1.10	8.87E-01
rs1830513	67287570	A	G	10	94	297	6	86	340	0.83	9.05E-02	0.14	0.11	1.29	0.96	1.75	1.72E-01
rs2863202	67296356	A	G	20	123	258	12	123	298	0.87	8.89E-02	0.20	0.17	1.25	0.97	1.61	2.07E-01
rs3762318	67309140	A	G	218	145	33	251	156	25	0.91	1.93E-01	0.27	0.24	0.86	0.69	1.08	8.16E-02
rs10489631	67313136	A	G	148	203	49	146	225	62	0.10	2.69E-01	0.38	0.40	1.12	0.91	1.37	2.01E-02
rs4655683	67323634	A	G	18	153	230	21	175	237	0.11	4.94E-01	0.24	0.25	0.92	0.73	1.16	1.19E-03
rs12041056	67339281	A	G	89	202	109	82	239	112	0.02	6.95E-01	0.48	0.47	1.04	0.85	1.27	9.11E-02
rs1884444	67345833	A	C	142	205	54	147	222	64	0.18	5.82E-01	0.39	0.40	1.06	0.87	1.30	7.24E-02
rs6687620	67360481	A	G	7	90	303	7	104	322	0.67	7.19E-01	0.13	0.14	0.95	0.71	1.27	2.36E-01
rs2064689	67365031	A	G	6	107	288	12	131	290	0.54	9.83E-02	0.15	0.18	0.80	0.61	1.05	8.52E-05
rs10489630	67374643	A	C	212	163	26	201	197	35	0.17	7.45E-02	0.27	0.31	1.22	0.98	1.51	7.07E-05
rs1004819	67382234	A	G	68	206	127	45	199	189	0.49	1.00E-04	0.43	0.33	1.48	1.21	1.82	1.54E-09
rs790631	67388943	A	G	181	183	36	199	199	35	0.13	7.51E-01	0.32	0.31	0.96	0.78	1.19	3.75E-01
rs7517847	67393690	A	C	229	147	22	185	191	57	0.49	5.84E-07	0.24	0.35	1.72	1.38	2.15	3.36E-13
rs2863212	67397137	A	G	343	57	1	366	64	3	0.91	5.84E-01	0.07	0.081	1.11	0.76	1.62	5.09E-01
rs7530511	67397408	A	G	3	77	321	5	83	345	1.00	8.11E-01	0.10	0.11	0.96	0.69	1.33	8.01E-01
rs10489629	67400370	A	G	164	189	48	119	225	89	0.36	5.79E-06	0.36	0.47	1.58	1.29	1.93	1.14E-10
rs2201841	67406223	A	G	129	212	60	203	187	43	0.99	2.92E-05	0.41	0.32	0.65	0.53	0.80	5.46E-10
rs11804284	67411275	A	G	3	72	325	3	81	349	0.47	8.70E-01	0.10	0.10	0.97	0.69	1.35	7.98E-01
rs12030948	67413786	A	C	78	213	104	75	209	147	0.96	4.20E-02	0.47	0.42	1.23	1.01	1.50	1.34E-03
rs11465804	67414547	A	C	362	36	1	347	78	2	0.28	1.39E-04	0.048	0.10	2.12	1.41	3.25	5.97E-10
rs10489628	67416128	A	G	37	176	188	53	214	166	0.21	1.32E-02	0.31	0.37	0.77	0.63	0.95	1.96E-04
rs11209026	67417979	A	G	0	26	374	1	58	372	0.42	7.95E-04	0.033	0.070	0.45	0.27	0.73	3.55E-11
rs6682033	67420691	A	G	270	118	13	250	162	20	0.33	6.55E-03	0.18	0.23	1.39	1.09	1.79	4.10E-04
rs1343151	67431150	A	G	21	142	238	41	209	183	0.09	1.69E-06	0.23	0.34	0.59	0.47	0.73	1.64E-11
rs10889675	67434237	A	C	8	92	300	3	110	316	0.046	1.00E+00	0.14	0.14	1.00	0.75	1.34	4.22E-01
rs10889677	67437141	A	C	63	210	128	44	186	203	0.88	1.51E-05	0.42	0.32	1.56	1.27	1.91	9.58E-11
rs7539328	67444624	A	G	37	115	243	53	160	219	0.01	2.01E-03	0.24	0.31	0.71	0.56	0.88	8.44E-07
rs11209032	67452113	A	G	63	180	158	41	176	216	0.56	3.49E-04	0.38	0.30	1.45	1.18	1.79	1.60E-09
rs1495965	67465529	A	G	112	202	87	142	225	66	0.13	2.04E-02	0.47	0.41	0.79	0.65	0.97	2.55E-06
rs924080	67472161	A	G	132	185	80	101	226	100	0.23	1.02E-02	0.43	0.50	1.30	1.06	1.58	3.83E-06
rs12131065	67481027	A	G	13	126	262	12	135	286	0.41	8.01E-01	0.19	0.18	1.04	0.81	1.34	3.89E-01
rs3790558	67489042	A	C	120	189	92	117	212	104	0.68	4.33E-01	0.47	0.48	1.08	0.89	1.32	6.51E-02
rs10489627	67491697	A	G	168	183	50	182	196	55	0.84	1.00E+00	0.35	0.35	1.00	0.82	1.23	1.98E-01
rs2066445	67493996	A	G	12	103	286	13	119	301	0.77	6.43E-01	0.16	0.17	0.94	0.71	1.22	8.06E-02
rs1495964	67506839	A	G	88	215	98	99	234	100	0.09	6.59E-01	0.49	0.50	0.96	0.79	1.16	6.72E-01
rs3790565	67523377	A	G	192	176	33	235	172	26	0.46	5.59E-02	0.30	0.26	0.81	0.65	1.01	1.50E-01
rs3790567	67534398	A	G	50	199	151	51	218	162	0.083	9.19E-01	0.37	0.37	1.01	0.82	1.24	6.17E-01
rs3828069	67551594	A	G	298	97	6	324	106	3	0.070	7.18E-01	0.14	0.13	0.94	0.70	1.27	1.98E-01
rs4297265	67564356	A	G	89	216	95	100	232	100	0.12	7.69E-01	0.49	0.50	0.97	0.80	1.18	5.15E-01
rs2270614	67568042	A	G	95	217	89	101	233	99	0.11	8.45E-01	0.49	0.50	1.02	0.84	1.24	5.15E-01
rs7555183	67572648	A	G	39	201	161	37	190	206	0.46	6.72E-02	0.35	0.30	1.22	0.99	1.50	8.90E-01

Table S2. Summary of family-based association test results in the non-Jewish CD, non-Jewish UC, Jewish CD, Jewish UC, and all IBD cohorts. Shown are the list of markers on chromosome 1, the over-transmitted allele, counts of transmitted (T) and untransmitted (U) alleles, and P-values computed using the empirical variance estimator implemented in the family-based association testing (FBAT) software package (<http://www.biostat.harvard.edu/~fbat/fbat.htm>) (S4, S5).

marker	Non-Jewish CD					Non-Jewish UC					Jewish CD					Jewish UC					All IBD				
	Over-trans	T	U	P value	Over-trans	T	U	P value	Over-trans	T	U	P value	Over-trans	T	U	P value	Over-trans	T	U	P value	Over-trans	T	U	P value	
rs3762318	C	192	162	1.26E-01	T	67	62	6.55E-01	C	36	31	5.58E-01	T	36	27	2.72E-01	C	327	299	2.63E-01					
rs7540900	C	160	134	1.50E-01	A	53	52	9.25E-01	A	28	26	7.93E-01	A	30	15	2.53E-02	C	262	248	5.35E-01					
rs4655683	G	296	260	1.55E-01	G	108	96	3.96E-01	A	34	27	3.62E-01	G	34	29	5.00E-01	G	476	426	1.10E-01					
rs11465770	C	141	101	1.08E-02	C	62	39	3.05E-02	C	20	16	5.05E-01	T	23	17	3.55E-01	C	241	183	4.85E-03					
rs11465791	A	77	73	7.41E-01	A	30	18	7.68E-02	A	22	20	7.52E-01	A	20	9	2.18E-02	A	154	122	5.41E-02					
rs2064689	G	278	237	9.00E-02	A	101	96	7.23E-01	G	24	23	8.86E-01	G	30	22	2.48E-01	G	439	390	1.02E-01					
rs6656929	A	325	265	1.48E-02	T	114	111	8.37E-01	T	43	33	1.97E-01	-	39	39	1.00E+00	A	521	471	1.27E-01					
rs10489630	T	322	265	1.88E-02	T	117	104	3.96E-01	T	38	34	6.28E-01	G	37	35	8.06E-01	T	525	448	1.61E-02					
rs1004819	T	354	252	3.60E-05	T	134	85	1.20E-03	T	54	34	1.24E-02	T	42	37	5.47E-01	T	591	418	6.06E-08					
rs790633	C	259	245	5.50E-01	C	120	91	4.03E-02	C	44	36	2.94E-01	C	46	39	4.73E-01	C	473	419	6.53E-02					
rs7517847	T	359	252	2.30E-05	T	126	109	2.71E-01	T	46	29	3.50E-02	G	42	37	5.00E-01	T	581	442	1.80E-05					
rs10489629	A	365	284	1.87E-03	A	135	116	2.70E-01	A	52	44	4.33E-01	G	44	42	8.21E-01	A	607	498	1.27E-03					
rs4655692	G	236	223	5.05E-01	G	102	68	1.22E-02	G	38	30	3.17E-01	G	39	32	4.13E-01	G	419	361	3.45E-02					
rs2201841	C	327	241	5.80E-04	C	139	83	3.21E-04	C	52	35	3.50E-02	C	43	38	5.69E-01	C	571	404	1.04E-07					
rs12070470	T	157	121	2.44E-02	T	67	46	5.42E-02	T	25	18	2.97E-01	C	28	24	5.64E-01	T	275	216	7.74E-03					
rs11465804	T	72	31	1.32E-04	T	36	15	2.70E-03	T	28	2	8.90E-05	G	12	8	3.71E-01	T	146	61	3.46E-09					
rs10489628	C	339	300	1.46E-01	T	119	115	8.08E-01	T	50	35	1.20E-01	C	43	42	9.06E-01	C	544	519	4.80E-01					
rs10789229	C	321	288	1.69E-01	T	121	97	1.24E-01	C	44	38	5.40E-01	T	45	23	1.05E-02	T	499	491	8.24E-01					
rs11209026	G	68	23	8.00E-06	G	34	10	2.97E-04	G	20	1	9.41E-04	A	9	6	4.91E-01	G	130	45	1.32E-10					
rs1343151	C	289	249	9.63E-02	C	111	85	8.51E-02	C	48	28	3.30E-02	C	34	24	1.89E-01	C	492	394	1.24E-03					
rs10889677	A	322	246	2.60E-03	A	136	82	3.35E-04	A	51	36	5.88E-02	A	42	39	7.32E-01	A	559	409	1.65E-06					
rs7539328	G	245	212	1.22E-01	A	77	71	6.31E-01	G	34	29	5.53E-01	G	36	23	9.06E-02	G	391	347	1.13E-01					
rs2863209	G	130	124	7.07E-01	A	59	33	1.08E-02	G	13	12	8.35E-01	A	16	13	5.32E-01	A	213	195	3.73E-01					
rs17303361	G	178	175	8.77E-01	A	77	58	9.95E-02	A	31	23	3.32E-01	G	36	29	3.54E-01	A	315	298	4.92E-01					
rs11209032	A	335	262	2.68E-03	A	148	90	3.57E-04	A	53	34	3.48E-02	A	41	38	7.50E-01	A	588	437	2.41E-06					
rs1495965	G	369	279	4.07E-04	G	152	113	1.74E-02	G	54	35	3.93E-02	A	47	46	9.21E-01	G	633	489	1.72E-05					
rs924080	T	323	271	4.20E-02	T	136	103	3.09E-02	T	62	30	1.88E-03	T	48	41	3.99E-01	T	577	452	9.74E-05					

Table S3. Association results from the case-control cohorts for the *IL23R* markers conditional on Arg381Gln. The P-values shown were obtained using the Cochran-Mantel-Haenszel test with strata defined based on Arg381Gln genotypes.

marker	location	non-Jewish P-value	Jewish P-value
rs1884444	67345833	9.52E-02	7.59E-01
rs6687620	67360481	9.86E-02	6.79E-01
rs2064689	67365031	6.53E-03	4.12E-01
rs10489630	67374643	8.58E-03	5.62E-01
rs1004819	67382234	7.77E-04	2.60E-03
rs790631	67388943	2.28E-01	8.79E-01
rs7517847	67393690	2.22E-04	3.60E-04
rs2863212	67397137	5.89E-01	5.30E-01
rs7530511	67397408	7.98E-01	7.45E-01
rs10489629	67400370	2.26E-03	4.52E-04
rs2201841	67406223	1.77E-04	3.27E-04
rs11804284	67411275	7.98E-01	8.66E-01
rs12030948	67413786	3.33E-05	3.53E-03
rs11465804	67414547	4.86E-01	1.20E-01
rs10489628	67416128	7.68E-04	5.87E-03
rs6682033	67420691	5.38E-04	4.85E-03
rs1343151	67431150	6.16E-04	2.30E-04
rs10889675	67434237	8.57E-02	1.93E-01
rs10889677	67437141	1.40E-04	2.21E-04

Table S4. Association results in the non-Jewish case-control cohort for Illumina HumanHap300 Genotyping BeadChip markers in and within 50kb of the *IL12RB1*, *IL23A*, and *IL12B* genes. The information from all International HapMap SNPs (*S1*) with minor allele frequencies > 0.05 within the *IL12RB1*, *IL23A*, and *IL12B* genes is captured by these genotyped markers with average pairwise r^2 values of 0.84, 1.0, and 0.92, respectively.

marker	Gene region	chromosome	position	CD			Control			HW-P	Allele-P		
				1	2	genotypes	11	12	22				
rs7255589	IL12RB1	19	17984965	A	G	4	80	459	3	71	470	8.58E-01	3.74E-01
rs91710	IL12RB1	19	18002123	A	G	111	266	165	122	252	170	1.22E-01	7.96E-01
rs393540	IL12RB1	19	18020220	A	G	224	249	70	237	235	72	2.58E-01	6.54E-01
rs4808739	IL12RB1	19	18020516	A	G	318	161	30	310	172	27	6.23E-01	8.30E-01
rs434815	IL12RB1	19	18028003	A	G	34	183	326	25	183	336	9.90E-01	3.54E-01
rs382410	IL12RB1	19	18029674	A	G	288	170	50	272	198	44	3.54E-01	5.51E-01
rs438421	IL12RB1	19	18037086	A	G	40	210	287	42	216	283	9.30E-01	7.35E-01
rs375947	IL12RB1	19	18041451	A	G	240	241	62	269	218	57	1.99E-01	1.29E-01
rs429774	IL12RB1	19	18047752	A	G	240	244	59	271	218	55	2.58E-01	1.17E-01
rs2305743	IL12RB1	19	18054191	A	G	23	188	332	25	165	354	3.10E-01	3.14E-01
rs7250425	IL12RB1	19	18062757	A	G	136	260	147	135	279	130	5.47E-01	4.93E-01
rs426132	IL12RB1	19	18067681	A	G	289	222	32	301	207	35	9.41E-01	6.95E-01
rs273512	IL12RB1	19	18085729	A	G	101	286	154	93	264	186	9.67E-01	9.09E-02
rs740691	IL12RB1	19	18095441	A	G	126	287	130	151	276	117	6.63E-01	1.12E-01
rs273493	IL12RB1	19	18101127	A	G	3	51	466	2	61	467	9.96E-01	5.76E-01
rs10783780	IL23A	12	54990419	A	G	492	47	2	487	54	3	2.68E-01	4.36E-01
rs2066808	IL23A	12	55024240	A	G	483	58	2	482	59	3	4.19E-01	8.55E-01
rs10056599	IL12B	5	158655488	A	C	314	203	26	336	173	35	5.19E-02	5.40E-01
rs7380834	IL12B	5	158668511	A	G	52	223	268	42	234	268	3.54E-01	6.73E-01
rs3181224	IL12B	5	158673428	A	G	430	106	7	419	116	9	7.66E-01	3.85E-01
rs2569253	IL12B	5	158683571	A	G	134	279	130	152	265	127	5.81E-01	3.91E-01
rs2569254	IL12B	5	158683827	A	G	19	166	355	14	158	371	5.60E-01	2.89E-01
rs1433048	IL12B	5	158688423	A	G	374	149	13	366	159	15	6.47E-01	4.90E-01
rs730691	IL12B	5	158688805	A	G	76	257	210	78	247	219	5.36E-01	7.90E-01
rs2546890	IL12B	5	158692478	A	G	116	289	123	143	242	152	2.25E-02	9.65E-01
rs7709212	IL12B	5	158696755	A	G	200	285	58	237	240	67	6.05E-01	2.27E-01
rs953861	IL12B	5	158705160	A	G	396	136	8	384	144	15	7.35E-01	2.08E-01
rs6869411	IL12B	5	158714182	A	G	222	263	58	252	229	63	3.21E-01	2.76E-01
rs12153168	IL12B	5	158718463	A	G	247	256	40	279	220	45	8.60E-01	2.22E-01

Supporting References and Notes

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